CLAIMS

1. A biosensor system for bioassay which comprises, as a set,

(A) polyethylene glycol-modified nanoparticles of a structural formula I:

$$(X–W^2–PEG–W^1–L)_x–PCL–(L–W^1–PEG–W^2–Y)_y \qquad (I)$$

in which

PCL stands for a free electron metal fine particle, metal oxide fine particle or semiconductor fine particle;

X stands for a functional group or functional moiety capable of binding to a biosensor chip surface;

Y stands for at least one group or moiety which is selected from the group consisting of C_1–C_6 alkyl, optionally protected functional groups which are useful for forming said functional group or functional moiety X, and functional moieties same as , or different from, X;

L stands for a linker or linkage portion linked to PCL;

W^1 and W^2 stand for single bonds or same or different linkers,

PEG stands for ethylene oxide units, $(–CH_2CH_2O–)_n$ (wherein n is an integer of 5 – 10,000),

W^2–PEG–W^1–L in $(X–W^2–PEG–W^1–L)_x$ and $(L–W^1–PEG–W^2–Y)_y$ may be same or different, and

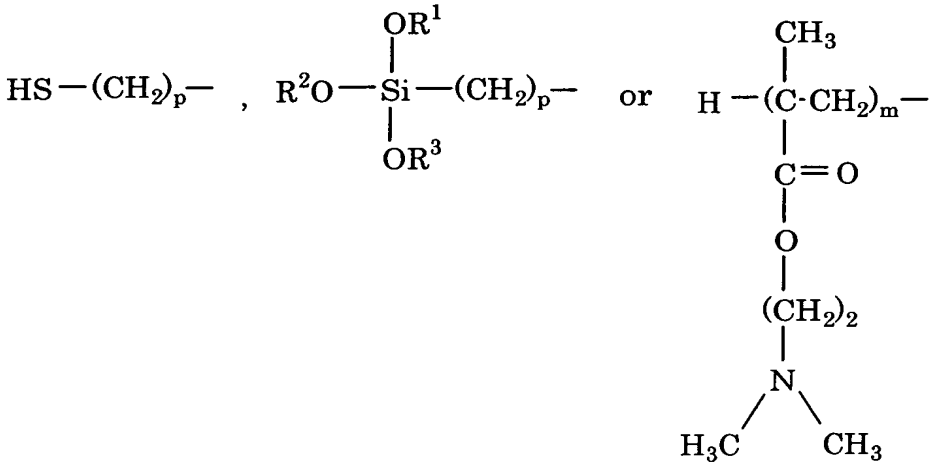
x and y are integers not less than 1 independently of each other, which together represent an integer sufficient for the PEG chains to cover the PCL surface in an aqueous medium and

(B) a biosensor chip having a surface to which above (A) particles can bind via X and which surface is made of glass or a material corresponding to that of PCL.

2. A biosensor system according to Claim 1, in which said (A) particles are carried on one surface of the (B) biosensor chip as the particles are linked to the biosensor chip surface via X, to substantially cover a part or whole area of said surface.

3. The biosensor system according to Claim 1, in which said (A) particles and (B) biosensor chip surface are used in a state of either being capable of binding to each other or being bound, the binding being such that can be replaced by an analyte in an aqueous medium due to competitive action of the analyte.

4. A biosensor system according to Claim 1, in which –L– in the structural formula I is a group selected from a group consisting of



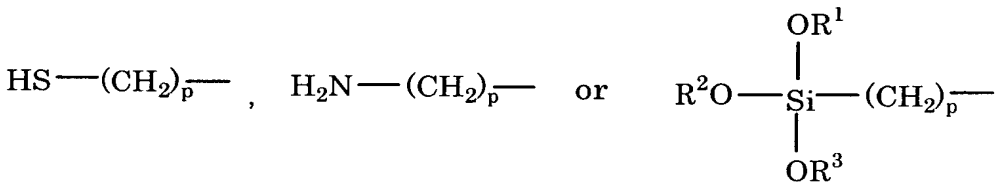
(in which p is independently an integer of 2 – 12, R^1, R^2 and R^3 each independently stands for C_1–C_6 alkyl, and m is an integer of 2 – 100); and

W^1 and W^2 each independently stands for a group selected from the group consisting of single bond, C_1–C_6 alkylene, –COO– (binding to methylene group in ethylene oxide unit via oxygen atom), –O–, –S–, –(C_1–C_6 alkylene) –COO–, –(C_1–C_6 alkylene) –O– and –(C_1–C_6 alkylene) –S–.

5. A biosensor system according to Claim 1, in which X in the structural formula I representing said (A) particle is a residue of a member forming a biological specific binding pair; and (B) sensor chip has a thin membrane surface made of a material corresponding to that constituting PCL in the structural formula I, said surface

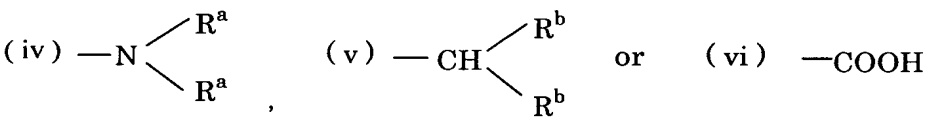
carrying the other member which forms said biological specific binding pair with said member X, either directly or via at least one of C_1–C_6 alkylene or $(-CH_2CH_2O-)_n$ (wherein n is an integer of 5 – 10,000).

6. A biosensor system according to Claim 1, in which X in the structural formula I representing said (A) particle stands for any one of the following groups



(in which p is an integer of 2 – 12 independently of each other; R^1, R^2 and R^3 each independently stands for C_1–C_6 alkyl); (B) sensor chip has a thin membrane surface made of any one of the materials forming PCL of the structural formula I or a glass surface; and said (A) particles and surface of (B) sensor chip are linked to each other via the functional group X, X having trialkoxysilyl where surface of (B) is made of glass.

7. A biosensor system according to Claim 5, in which Y in the structural formula I representing said (A) particles is a group selected from those of the following formulae:



(in which R^a each independently stands for hydrogen or C_1–C_6 alkyl; R^b each independently stands for a C_1–C_6 alkyloxy; or the two R^b's together stand for an atomic group forming oxy or an optionally C_1–C_6 alkyl-substituted ethylene group).

8. A biosensor system according to Claim 1, in which x + y in the structural formula I representing said (A) particles is an integer corresponding to 0.1 – 0.5 per 1 nm^2.

9. A biosensor system according to Claim 1, in which PCL in said (A) particle has an average cross-sectional length of 5 – 500 nm.

10. A polyethylene glycol-modified nanoparticle of a structural formula I

$$(X–W^2–PEG–W^1–L)_x–PCL–(L–W^1–PEG–W^2–Y)_y \qquad (I)$$

in which

PCL stands for a free electron metal fine particle, metal oxide fine particle or semiconductor fine particle;

X stands for a functional group or functional moiety capable of binding to a biosensor chip surface;

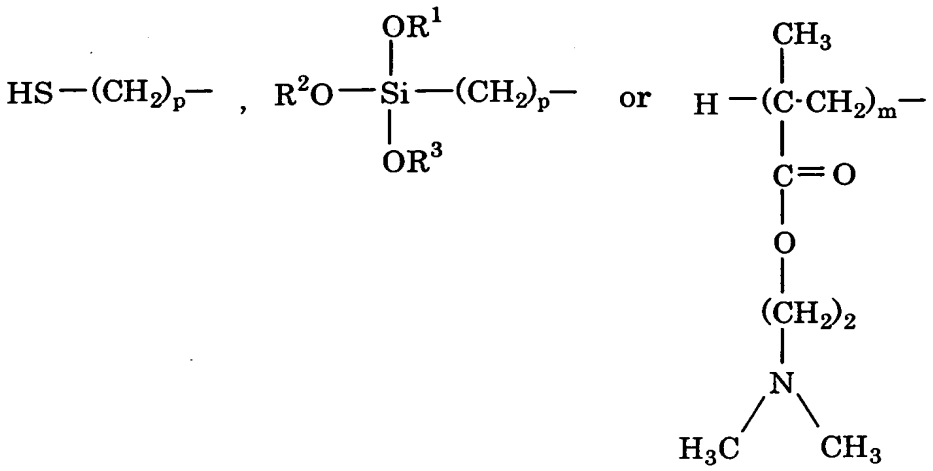
Y stands for at least one group or moiety which is selected from the group consisting of C_1–C_6 alkyl, optionally protected functional groups which are useful for forming said functional group or functional moiety X, and functional moieties same as , or different from, X;

L stands for a linker or linkage portion linked to PCL;

W^1 and W^2 stand for single bonds or same or different linkers,

PEG stands for ethylene oxide units, $(–CH_2CH_2O–)_n$ (wherein n is an integer of 5 – 10,000),

W^2–PEG–W^1–L in $(X–W^2–PEG–W^1–L)_x$ and $(L–W^1–PEG–W^2–Y)_y$ may be same or different, X being a residue of a member to form a biological specific binding pair, Y being a group other than the residue of the member forming said biological specific binding pair, L standing for a group of the formula



(in which p is an integer of 2 – 12, R^1, R^2 and R^3 each independently stands for C_1–C_6 alkyl, and m is an integer of 2 – 100);
x + y is a number corresponding to 0.1 – 0.5 per 1 nm^2 of the PCL surface, (x/ x + y) × 100 being an integer of 1 – 99, and the average dimension of cross-section of the PCL is 5 – 500 nm.

11. A polyethylene glycolated nanoparticle according to Claim 10, in which said member to form a biological specific binding pair is a residue derived from a substance selected from a group consisting of monosaccharide or oligosaccharide, antigen or hapten, substrate, hormone and oligonucleotide.

12. A method of detecting an analyte in a biological fluid, which comprises:

(a) preparing polyethylene glycol-modified nanoparticles as described in Claim 10,

(b) preparing a biosensor chip having a thin membrane surface made of a material corresponding to that forming PCL of the nanoparticles, said surface carrying, either directly or via at least a C_1–C_6 alkylene or $(-CH_2CH_2O-)_n$ (wherein n is an integer of 5 – 10,000), a member which is to form a biological specific binding pair with the other member present in X of said nanoparticles,

(c) contacting said particles (a) and biosensor chip (b) with a biological fluid which is suspected to contain either one of the members capable of forming the biological specific binding pair as an

analyte,

(d) determining the change in the extent of linkage of the particles (a) to the biosensor chip (b) surface caused by the competitive action of the analyte and

(e) using the change as an index of the analyte concentration in said biological fluid.

13. A detection method according to Claim 12, in which the change in the extent of linkage of the particles (a) to the biosensor chip (b) surface in the step (d) is detected as a change in surface plasmon resonance spectrum.

14. A detection method according to Claim 12, in which the pair formed by two members capable of forming a biological specific binding pair is selected from the group consisting of sugar - lectin, antigen or hapten - antibody, substrate - enzyme, hormone - receptor protein, oligonucleotide - either oligonucleotide or polynucleotide which contain complementary chain sequence of the first oligonucleotide.

15. A detection method according to Claim 12, in which said particles (a) and the biosensor chip (b) surface form biological specific binding pairs and are linked in advance.